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**Journal of Occupational and Environmental Medicine**

Volume 43 • Number 4 • April 2001

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## ORIGINAL ARTICLES

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### **Occupational Risk Factors for Brain Cancer: A Population-Based Case-Control Study in Iowa**

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A number of occupations and industries have been inconsistently associated with the risk of brain cancer. To further explore possible relationships, we conducted a population-based case-control study of brain glioma in the state of Iowa, involving 375 histologically confirmed incident cases and 2434 population-based controls. Among men, the industries and/or occupations that had a significantly increased risk for employment of more than 10 years included roofing, siding, and sheet metalworking; newspaper work; rubber and plastics products, particularly tires and inner tubes; miscellaneous manufacturing industries; wholesale trade of durable goods, grain, and field beans; cleaning and building service occupations; miscellaneous mechanics and repairers; and janitors and cleaners. Subjects who worked in plumbing, heating, and air conditioning; electrical services; gasoline service stations; and military occupations also experienced a significantly increased risk. Among women, significant excess risk was observed for occupations in agricultural services and farming, apparel and textile products, electrical and electronic equipment manufacturing, various retail sales, record-keeping, and restaurant service. Workers in industries with a potential for gasoline or motor exhaust exposures experienced a non-significant excess risk of brain glioma.

#### **Introduction**

Brain cancer incidence and mortality have been increasing in many industrialized countries, particularly among elderly people. Improved diagnosis and better access to medical care, which may result in more

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accurate case finding, seem unable to entirely explain the increasing trend. <sup>[1]</sup> Established risk factors for brain cancer, such as genetic predisposition and ionizing radiation, can explain only a small proportion of the disease. <sup>[2]</sup> Conventional lifestyle factors, such as tobacco smoking, alcohol drinking, and dietary intakes, have not been or are only modestly associated with brain cancer risk. <sup>[3]</sup>

A number of industries, occupations, and **occupational** exposures have been associated with the risk of brain cancer, <sup>[2]</sup> albeit inconsistently. These include agriculture, nuclear power production, rubber manufacturing and fabrication, and the petrochemical industry. Increased risk has also been observed among people working in electricity-related occupations and health professions, including physicians, dentists, nurses, pathologists, and veterinarians.

Most epidemiological studies of occupation and brain cancer risk have relied on mortality data. Even though the risk of brain cancer associated with **occupational** exposures may vary by histological type, few studies have investigated risk in that way <sup>[4][5]</sup> Brain gliomas, in particular, appear to be more related to **occupational** risk factors than other types of brain cancer, as summarized by Schlehofer et al <sup>[6]</sup> In addition, few studies have investigated the association between brain cancer and **occupational** exposures in women. To further examine the association between **occupational** and industrial exposures and the risk of brain cancer in men and women, we analyzed the data from a population-based case-control study of brain glioma in the state of Iowa.

## Materials and Methods

### *Study Population*

As described elsewhere, <sup>[7]</sup> a total of 412 persons with histologically confirmed glioma, aged 40 to 85, were identified by the State Health Registry of Iowa from January 1984 to December 1987. Those eligible to participate were residents of Iowa and had no previous diagnosis of a malignant neoplasm. Of the 412 persons, 375 (91%) with glioma participated in the study (201 male and 174 female), including 193 with glioblastomas (International Classification of Diseases for Oncology [ICD-O] code 9440), 114 with astrocytomas (ICD-O 9400), 27 with fibrillary astrocytomas (ICD-O 9420), 12 with mixed gliomas (ICD-O 9382), 6 with gemistocytic astrocytomas (ICD-O 9411), 5 with malignant gliomas not otherwise specified (ICD-O 9380), and 18 with other histologic findings. These patients with glioma were part of a larger study that also included patients with cancers of the bladder, kidney, pancreas, colon, and rectum.

A total of 2434 population-based controls (1601 male and 833 female) were frequency-matched by sex and 5-year age group to all cases in the larger study. The matching ratio for brain glioma cases was approximately 6.5:1. Control subjects younger than 65 years were randomly selected from computerized state driver's license records. Control subjects 65 years and older were selected from US Health Care Financing Administration listings. As with the cases, persons with a previous cancer diagnosis were excluded from consideration as controls. The participation rate was 82% for controls younger than 65, and 80% for those aged 65 and older.

### *Data Collection*

After obtaining physician consent, the glioma patients or their next of kin were first contacted by mail and then by telephone. A postal questionnaire was used to collect detailed information. Of the 375 respondents, 279 (74.4%) were proxies, composed of 184 spouses, 21 siblings, 55 offspring, and 19

others, mostly blood relatives or in-laws.

Respondents were asked to report all jobs held by the patient for 5 years or longer since age 16. For each job reported, information was elicited about the job title, type of business or industry, year when each job began and ended, and activities and duties associated with the job. In addition, respondents were asked to report the usual occupation held during most of the patient's adult life and for the main activities and duties on the job. Industries and job titles obtained from the **occupational** history were coded according to the Standard Industry Classification (SIC) <sup>[8]</sup> and the Standard **Occupational** Classification Manual (SOC) <sup>[9]</sup> schemes. Information on demographic factors, residential history, smoking, past medical history, first-degree family history of brain and other cancers, and other factors was also collected.

### Data Analysis

Risks for brain cancer associated with jobs held for at least 5 years were calculated separately for men and women, using unconditional logistic regression models. Odds ratios (ORs) and 95% confidence intervals were calculated using SAS statistical software. <sup>[10]</sup> ORs were calculated for all 2-, 3-, and 4-digit SOC and SIC codes when there were at least three exposed cases in one of the sexes. We also evaluated the risk of brain cancer by duration of employment (<10 years and  $\geq 10$  years) in various SOC and SIC categories. The reference category was composed of subjects not employed in the occupation or industry of interest.

The following potential confounders, which showed an impact on the observed ORs, were included in the final regression models: age (40 to 54, 55 to 64, 65 to 74, 75 to 85 years), body mass index (<24, 24 to 26,  $\geq 26$  kg/m<sup>2</sup>), level of education ( $\leq 8$ , 9 to 11, 12 to 15,  $\geq 16$  years), frequency of strenuous or moderate exercise ( $\geq 1$  time/day, 2 to 6 times/week, 1 to 4 times/month, <1 time/month), duration of living in a residence served by chlorinated surface water (0, 1 to 19, 20 to 39,  $\geq 40$  years), and having a first-degree relative with brain cancer (yes/no). Additional adjustment for population size of places of residence (based on 1980 census) averaged over a lifetime, and other types of cancer in a first-degree relative, did not result in a material change to the observed associations, and these factors were not included in the final models.

### Results

As noted above, controls were matched by age to all cases in the larger study, and the age distribution of the controls therefore differed from that of the glioma cases (Table 1). Because age is a risk factor for brain cancer, it was controlled for in all subsequent analyses. A significantly higher proportion of glioma patients than controls reported having a first-degree relative with brain cancer among both the men and women.

**Table 1. Number and Proportion (%) of Brain Cancer Cases and Controls Based on Selected Characteristics in a Case-Control Study of Brain Cancer in Iowa**

Factor	Men				Women			
	Case		Control		Case		Control	
	n	%	n	%	n	%	n	%

Age								
40-54	56	27.9	149	9.3	35	20.1	93	11.2
55-64	69	34.3	358	22.4	41	23.6	190	22.8
65-74	55	27.4	629	39.3	67	38.5	276	33.1
75-85	21	10.5	465	29.0	31	17.8	274	32.9
Body mass index								
<24	47	23.4	366	22.9	61	35.1	307	36.9
24-26	69	34.3	545	34.0	51	29.3	196	23.5
>26	66	32.8	581	36.3	43	24.7	240	28.8
Unknown	19	9.5	109	6.8	19	10.9	90	10.8
Years of education								
≤ 8	45	22.4	392	24.5	31	17.8	115	13.8
9-11	25	12.4	203	12.7	17	9.8	119	14.3
12-15	59	29.4	589	36.8	64	36.8	333	40.0
≥ 16	68	33.8	407	25.4	59	33.9	261	31.3
Unknown	4	2.0	10	0.6	3	1.7	5	0.6
Frequency for strenuous or moderate exercise								
≥ 1/day	32	15.9	281	17.6	27	15.5	160	19.2
2-6/week	47	23.4	402	25.1	43	24.7	249	29.9
1-4/month	33	16.4	216	13.5	34	19.5	132	15.8
<1/month	63	31.3	553	34.5	50	28.7	179	21.5
Unknown	26	12.9	149	9.3	20	11.5	113	13.6
Duration at surface chlorinated water source								
0	125	62.2	1063	66.4	102	58.6	509	61.1
1-19	45	22.4	351	21.9	47	27.0	197	23.7
20-39	16	8.0	103	6.4	18	10.3	65	7.8
≥ 40	15	7.5	84	5.3	7	4.0	62	7.4
First-degree relatives with brain cancer								
No	180	89.5	1,501	93.7	153	87.9	790	94.8
Yes	9	4.5	17	1.1	11	6.3	10	1.2
Unknown	12	6.0	83	5.2	10	5.8	33	4.0

Table 2 presents industries or occupations, by 2-, 3-, or 4-digit SIC and SOC codes, with significant associations for brain cancer in the men, either overall or in one of the duration categories. A significantly increased risk was observed among those working in plumbing, heating, and air conditioning; roofing, siding and sheet metalworking; newspapers; rubber and plastic product manufacturing, particularly tires and inner tubes; miscellaneous manufacturing industries; electrical services; wholesale trade of farm-products; gasoline service stations; and the military. Workers in

cleaning and building service occupations, miscellaneous mechanical and repair occupations, and janitors and cleaners (especially those with more than 10 years of experience) also experienced a significantly increased risk. A significantly increased risk was also observed for financial officers, clergy, salespersons, guards, supervisors in construction and extractive occupations, and material-moving equipment operators.

**Table 2. Statistically Significant Associations Between Brain Cancer and Duration of Employment by Industry or Occupation Among Men**

Industry/Occupation	All*			<10 Years*			≥ 10 Years*		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Industry (SIC code)									
Plumbing, heating, air conditioning (171)	3 /11	2.8	0.7 - 10.9	2 /1	21.6	1.8 - 259	1 /10	0.9	0.1 -8.0
Roofing, siding, and sheet metalwork (1761)	4 /2	22.3	3.2 - 153	1 /0			3 /2	11.1	1.5 - 83.1
Newspapers (2711)	5 /11	5.8	1.9 - 17.9	0 /3			5 /8	8.2	2.4 - 27.5
Rubber and plastics products (30)	4 /6	4.9	1.2 - 19.2	0 /1			4 /5	5.3	1.3 - 21.6
Tires and inner tubes (3011)	3 /4	4.8	0.9 - 24.7	0 /1			3 /3	5.3	1.0 - 29.9
Miscellaneous manufacturing industries (39)	3 /5	8.2	1.8 - 38.0	1 /2	5.8	0.4 - 77.0	2 /3	10.0	1.5 - 66.6
Electrical service (4911)	5 /8	5.7	1.7 - 18.7	2 /0			3 /8	3.1	0.8 - 12.3
Wholesale trade: durable goods (50)	11 /41	2.4	1.1 -4.9	2 /14	1.3	0.3 -6.1	9 /27	2.9	1.3 -6.7
Wholesale trade: farm products (515)	6 /8	5.8	1.9 - 18.4	3 /1	17.3	1.6 - 185	3 /7	3.7	0.9 - 15.8
Wholesale trade: grain and field beans (5153)	4 /4	7.6	1.8 - 33.1	1 /1	8.3	0.5 - 149	3 /3	7.4	1.3 - 40.8
Gasoline service stations (5541)	6 /24	2.4	0.9 -6.3	3 /9	4.8	1.2 - 19.3	3 /15	1.5	0.4 -5.6
Occupation (SOC code)									
Other financial officers (1419)	3 /6	2.5	0.6 - 11.7	0 /4			3 /2	9.9	1.4 - 70.7
Clergy (2042)	4 /7	3.8	1.0 - 14.5	0 /0			4 /7	3.8	1.0 - 14.5
Salespersons, commodities (434, 435)	15 /74	1.9	1.0 -3.5	6 /19	2.6	0.9 -7.0	9 /55	1.6	0.8 -3.5

Guards (514)	3 /7	4.5	1.1 - 18.8	2 /3	6.9	1.0 - 46.7	1 /4	2.7	0.3 - 26.3
Cleaning and building service occupations (524)	9 /42	2.0	0.9 -4.4	2 /16	1.0	0.2 -4.6	7 /26	2.8	1.1 -6.9
Janitors and cleaners (5244)	8 /27	2.9	1.2 -7.0	1 /11	0.9	0.1 -7.2	7 /16	4.5	1.7 - 12.1
Miscellaneous mechanics and repairers (617)	8 /25	2.7	1.2 -6.4	2 /11	1.5	0.3 -7.2	6 /14	3.7	1.3 - 10.3
Supervisors, construction and extractive occupations (63)	6 /22	2.8	1.1 -7.3	1 /2	5.2	0.4 - 63.1	5 /20	2.5	0.9 -7.2
Material-moving equipment operators (831)	4 /17	2.0	0.6 -6.5	3 /4	8.2	1.6 - 41.7	1 /13	0.6	0.1 -4.8
Military occupation (91)	5 /25	1.8	0.7 -5.1	4 /14	3.5	1.1 - 11.2	1 /11	0.6	0.1 -4.6

\* Ca/Co, cases/controls; OR, odds ratios adjusted for age, body mass index, level of education, exercise, duration at surface chlorinated areas, and first-degree relative with brain cancer; CI, confidence interval; SIC, Standard Industry Classification; SOC, Standard Occupational Classification Manual.

The statistically significant associations among women for industries or occupations with three or more exposed subjects for which ORs for brain cancer were 2.0 or greater for at least one duration category are presented in Table 3. Employment in the agricultural industry, the apparel and textile industry, electrical and electronic equipment, department stores, and other retail industries was associated with a significantly increased risk of brain cancer for women. Salespersons, record clerks, waiters and waitresses, and farmers were also associated with a significantly increased risk. Further evaluation of the association, by duration of employment, shows that the observed significant associations among women, except for supervisors in retail sales occupations, occurred among those who worked for longer periods of time in these industries and occupations.

**Table 3. Statistically Significant Associations Between Brain Cancer and Industry or Occupation Among Women**

Industry/Occupation	All <sup>a</sup>			<10 Years <sup>a</sup>			≥ 10 Years <sup>a</sup>		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Industry (SIC code)									
Agriculture (01, 02)	9 /14	3.4	1.4 -8.5	2 /2	3.6	0.5 - 27.7	7 /12	3.4	1.3 -9.2
Apparel and other textile products (23)	4 /7	4.9	1.3 - 18.3	0 /4		4 /3	10.4	2.1 - 50.7	
Electrical and electronic equipment	5 /9	3.3	1.0 - 10.2	2 /6	1.8	0.4 -9.3	3 /3	6.8	1.3 - 36.6

(36)									
Department stores (5311)	8 /23	1.9	0.8 -4.6	1 /10	0.6	0.1 -4.9	7 /13	2.9	1.1 -7.7
Miscellaneous retail (59)	6 /21	1.7	0.6 -4.4	1 /10	0.5	0.1 -3.9	5 /11	3.2	1.0 - 10.0
Drug stores and proprietary (5912)	4 /7	3.8	1.0 - 14.2	0 /2		4 /5	6.0	1.5 - 24.8	
Occupation (SOC code)									
Supervisors: sales occupations, retail (403)	4 /15	1.3	0.4 -4.2	3 /3	5.7	1.0 - 32.0	1 /12	0.4	0.0 -3.0
Sales occupations, retail (43)	13 /36	2.4	1.2 -4.8	1 /12	0.6	0.1 -4.6	12 /24	3.3	1.5 -7.1
Salespersons, commodities (434, 435)	11 /22	3.3	1.5 -7.4	0 /10		11 /12	6.2	2.5 - 15.0	
Record clerks (469)	3 /7	1.5	0.3 -6.7	0 /5		3 /2	7.1	1.1 - 45.0	
Waiters and waitresses (5213)	4 /16	1.2	0.4 -3.9	0 /10			4 /6	3.8	1.0 - 14.8
Farm occupations (561)	4 /4	4.1	1.0 - 17.9	1 /2	1.6	0.1 - 19.2	3 /2	7.3	1.1 - 48.1
General farmworkers (5612)	4 /1	13.4	1.4 - 126	1 /1	2.7	0.2 - 46.1	3 /0		

\* For definition of abbreviations, see Table 2.

Table 4 presents the associations among men for industries and occupations with three or more exposed subjects in which ORs for brain cancer were 2.0 or greater overall or in one of the duration categories, but where the confidence intervals included the null value (1.0). Farm operators and managers, particularly farmers, had an increased risk based on 53 exposed cases and 426 exposed controls. A number of industries and occupations with the potential for solvent or gasoline exposure also experienced a not significantly increased risk, including trucking, automotive dealers and service stations, miscellaneous repair services, transportation occupations, and garage and service station-related occupations. Electrical and electronic equipment repairers also experienced a not significantly increased risk of brain cancer.

**Table 4. Risk (OR > 2.0) of Brain Cancer by Industry or Occupation Among Men (Based on Three or More Exposed Cases)**

Industry/Occupation	All*			<10 Years*			≥ 10 Years*		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Industry (SIC code)									
Special trade	13 /68	1.7	0.9 -3.2	3 /13	2.6	0.7 -	10 /55	1.5	0.7 -3.1

contractors (17)						10.0			
Railroad transportation (40)	5 /33	1.4	0.5 -3.9	2 /9	2.5	0.5 - 12.7	3 /24	1.1	0.3 -3.9
Trucking and warehousing (42)	13 /56	1.8	0.9 -3.5	3 /11	2.7	0.7 - 10.7	10 /45	1.6	0.8 -3.4
Automotive dealers and service stations (55)	8 /43	1.8	0.8 -4.1	3 /14	3.3	0.9 - 12.2	5 /29	1.4	0.5 -3.9
Miscellaneous retail (59)	3 /30	0.7	0.2 -2.4	2 /9	2.3	0.4 - 12.8	1 /21	0.3	0.0 -2.2
Miscellaneous repair shops (769)	3 /16	1.9	0.5 -6.9	0 /3			3 /13	2.5	0.7 -9.4
Religious organizations (866)	4 /10	3.2	0.9 - 11.5	0 /1			4 /9	3.4	0.9 - 12.4
Occupation (SOC code)									
Accountants, auditors, and other financial specialists (141)	6 /22	1.7	0.6 -4.8	0 /6			6 /16	2.5	0.8 -7.3
Religious workers (204)	4 /8	3.5	0.9 - 13.1	0 /0			4 /8	3.5	0.9 - 13.1
Insurance, securities, real estate, and business service sales (41)	4 /18	1.5	0.5 -5.1	1 /1	6.9	0.3 - 177	3 /17	1.2	0.3 -4.7
Farm operators and managers (55)	54 /442	1.3	0.9 -1.8	7 /35	1.9	0.8 -4.5	47 /407	1.2	0.8 -1.8
Farmers (551)	53 /426	1.3	0.9 -1.9	7 /34	1.9	0.8 -4.7	46 /392	1.2	0.8 -1.8
Electrical and electronic equipment repairers (615)	4 /23	1.4	0.4 -4.4	3 /4	4.7	0.8 - 25.8	1 /19	0.5	0.1 -3.9
Other construction trades (646, 647)	3 /8	2.3	0.6 -9.5	0 /3			3 /5	3.3	0.7 - 15.3
Metal and plastic work machine operators (751, 752)	5 /23	2.1	0.8 -5.9	1 /9	1.3	0.2 - 10.8	4 /14	2.5	0.8 -8.3
Transportation occupations (82)	21 /131	1.4	0.8 -2.4	7 /37	2.1	0.9 -5.1	14 /94	1.2	0.6 -2.2
Garage and service station-related occupations (873)	4 /20	2.3	0.7 -7.3	2 /8	3.3	0.6 - 16.9	2 /12	1.8	0.4 -8.6

\* For definition of abbreviations, see Table 2.

Table 5 presents the non-significant excess risks among women. Several industries or occupations had a higher risk of brain cancer associated with longer duration of employment, including general merchandise store occupations; agricultural and related occupations; and precision textile, apparel, and furnishings occupations. Female farmers also experienced an increased risk.

**Table 5. Risk (OR > 2.0) of Brain Cancer by Industry or Occupation Among Women (Based on Three or More Exposed Cases)**

Industry/Occupation	All <sup>a</sup>			<10 Years <sup>a</sup>			≥10 Years <sup>a</sup>		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
Industry (SIC code)									
Meat products (201)	4 /13	1.9	0.6 -6.0	3 /8	2.1	0.5 -8.2	1 /5	1.4	0.2 -13.3
General merchandise stores (53)	9 /31	1.7	0.7 -3.7	2 /15	0.8	0.2 -3.6	7 /16	2.5	0.9 -6.4
Nursing and personal care facilities (805)	3 /20	0.8	0.2 -2.9	2 /6	2.3	0.4 -12.6	1 /14	0.3	0.0 -2.7
Occupation (SOC code)									
Supervisors: marketing and sales occupations (40)	4 /20	0.9	0.3 -2.8	3 /5	2.9	0.6 -13.5	1 /15	0.3	0.0 -2.3
Cleaning and building service occupations (524)	3 /20	0.9	0.3 -3.3	3 /8	2.2	0.5 -9.1	0 /12		
Farmers (working proprietors) (551)	4 /9	2.5	0.7 -8.9	1 /1	4.7	0.3 -78.9	3 /8	2.2	0.5 -9.0
Other agricultural and related occupations (56)	5 /7	2.9	0.9 -9.8	1 /2	1.6	0.1 -19.3	4 /5	3.6	0.9 -14.1
Precision production occupations (68)	7 /18	2.3	0.9 -5.7	3 /7	2.3	0.6 -9.2	4 /11	2.3	0.7 -7.6
Precision textile, apparel, and furnishings workers (685)	3 /6	3.5	0.8 -15.1	0 /0			3 /6	3.5	0.8 -15.1
Machine operators and tenders (75, 76)	7 /28	1.5	0.6 -3.5	3 /8	2.1	0.5 -8.3	4 /20	1.2	0.4 -3.7
Machine operators and tenders; assorted materials (766, 767)	5 /10	2.4	0.8 -7.5	3 /5	2.9	0.7 -12.6	2 /5	1.9	0.3 -11.0
Assemblers (772)	5 /13	1.8	0.6 -5.3	2 /5	2.1	0.4 -11.0	3 /8	1.6	0.4 -6.5

\* For definition of abbreviations, see Table 2.

## Discussion

In this population-based case-control study of brain gliomas among men and women, we observed several statistically significant associations between employment in certain industries/occupations and brain gliomas. These include some that have been previously noted and some new observations. Our major findings are summarized and discussed below.

We found a significantly increased risk of brain cancer for agricultural industry and farm occupations among women and a not significantly increased risk for male and female farmers. An increased risk of brain cancer among farmers has been reported by a majority of the earlier studies, as reviewed by others.<sup>[2][11]</sup> Although two early studies found no increased risk among female farmers,<sup>[6][12]</sup> two more recent studies found an increased risk of gliomas in female farmers.<sup>[13][14]</sup> Exposure to pesticides has been suggested as a major risk factor for brain cancer among farmers. Specifically, the use of insecticides and fungicides has been linked to the risk of brain cancers.<sup>[15][16]</sup> Higher levels of pesticides have been reported in the adipose tissue of glioblastoma patients than in controls.<sup>[17]</sup> These observations support the hypothesis that agricultural exposure to pesticides may increase the risk of brain cancer.

Industries producing rubber and miscellaneous plastic products, particularly tires and inner tubes, were associated with an increased risk of brain cancer in this study. An increased risk of brain cancer has been reported elsewhere for rubber industry workers, particularly those involved in the manufacture of tires.<sup>[2]</sup><sup>[14]</sup> Workers producing plastic materials have also been found to have an increased risk of brain cancer.<sup>[18][19]</sup> Workers in the rubber and plastic industries are exposed to a variety of **occupational** hazards in various phases of the complex manufacturing process, such as antioxidants, accelerators, plasticizers, extenders, softeners, and carbon black. Many of the compounds or their impurities have been suspected or shown to cause cancer in humans.<sup>[20][21]</sup> An increased risk of brain cancer has been associated with exposure to materials involved in plastics manufacture, including polyethylene, polystyrene, polyurethane, polyvinyl chloride,<sup>[19]</sup> and vinyl chloride.<sup>[22]</sup>

A number of industries and occupations that have a potential for exposure to gasoline or solvents also showed an increased risk of brain cancer in this study, including the trucking, automotive dealer/service station, and repair service industries and the transportation, garage/service station, cleaning and building service, and machine operating/tending occupations. Previous studies have reported an elevated risk of brain cancer in workers or subgroups of workers in the petrochemical industry.<sup>[2]</sup> The observations, however, have been inconsistent. Workers in the petrochemical industry are potentially exposed to both aromatic and aliphatic petroleum hydrocarbons, but no specific carcinogen has been implicated.<sup>[2]</sup> Earlier studies also reported an increased risk of brain cancer among automobile mechanics, chemical manufacturing workers, mechanics and repairers, and machinists.<sup>[23][24]</sup> These workers may have been exposed to solvents, lubricating oils, and hydrocarbons.<sup>[25]</sup> Various organic solvents have previously been associated with the risk of brain cancer, particularly gliomas.<sup>[26][27][28]</sup>

Occupations in electrical services, and electrical and electronic equipment, were significantly associated with an increased risk of brain cancer in this study. Earlier studies, although inconsistent, have reported elevated brain cancer risk associated with a variety of electricity-related occupations, including electrical or electronic engineers, teachers of electronics, electrical technicians and assemblers, and electrical

workers in manufacturing industries.<sup>[2] [29] [30] [31] [32]</sup> The interpretation of the observed association, however, is still uncertain. It is currently unknown whether the increased risk of brain cancer observed among electrical workers is linked to magnetic or electrical fields or exposure to hazards such as organic solvents, metal fumes, or polychlorinated biphenyls.<sup>[2]</sup>

Industries producing apparel and other textile products showed a significantly increased risk of brain cancer among women. In terms of occupation, precision textile, apparel, and furnishing workers also showed a non-significantly increased risk of brain cancer among women. These findings are consistent with earlier epidemiological studies that reported an increased risk of brain cancer in textile workers,<sup>[33] [34] [35]</sup> wool workers,<sup>[14] [36]</sup> and yarn and thread makers.<sup>[37]</sup> Textile workers may be exposed to various chemicals in processing fabrics,<sup>[25]</sup> including dyes and formaldehyde, some of which have been associated with brain cancer risk.<sup>[38] [39]</sup>

We observed a significantly increased risk of brain cancer in plumbing, heating, and air conditioning occupations and in the roofing, siding, and sheet metalworking industries. An earlier study<sup>[40]</sup> also reported an excess of brain and central nervous system tumors among plumbers and pipefitters. Plumbers and pipefitters encounter many hazardous materials, including asbestos, metal fumes, and gases from welding, brazing, and soldering and solvents used to join plastic pipe.

Caution should be exercised in interpreting our study results. Many observations are based on small numbers; therefore, chance cannot be ruled out as the explanation for the observed associations. In addition, some significant associations would be expected by chance alone, because many comparisons were made by occupation and industry.

Other potential limitations may influence the interpretation of our study findings. One concern is the use of proxy respondents for patients who were deceased or too ill to respond directly. As discussed elsewhere,<sup>[7]</sup> because proxy respondents accounted for about 74.4% of the cases, but essentially none of the controls, differential responses from proxy and direct respondents could have resulted in data quality differences between the cases and controls. This is a common concern in studies of brain cancer, given the nature of the disease and its rapid progression. However, earlier studies have shown that the industries and occupations reported by study subjects or their next of kin were in good agreement with industry personnel records.<sup>[41] [42] [43] [44] [45]</sup> Our study findings are consistent with earlier studies regarding associations with agricultural, rubber, electrical and electronic, and textile industries and with industries having the potential for exposure to gasoline or solvents. This suggests that differential recall by patients and controls or self- and proxy-respondents is an unlikely explanation for the observed associations.

Selection bias is an unlikely explanation for the observed association between various occupations and industries and brain cancer risk in our study. The population-based controls were randomly selected from the general population of Iowa using driver's license listings and rosters of the US Health Care Financing Administration. The population-distribution of individuals aged 40 to 64 years with drivers' licenses in Iowa parallels census enumeration data with respect to county of residence, 5-year age groups, urbanity, and sex, suggesting an unbiased sampling framework.<sup>[46]</sup> The US Health Care Financing Administration listings provide an estimated 98% coverage of the US population older than age 64, and this source has been used successfully in selecting controls in various population-based case-control studies in the United States.

Several characteristics of our study could strengthen the interpretation of our results. In this population-based case-control study, cases included persons with histologically confirmed incident brain gliomas, and information regarding lifetime job exposure history and other potential risk factors was collected from study subjects or their next of kin. The relatively high response rates in both the case and control groups also lend confidence to our study findings. Limitations of some of the earlier studies include the

use of mortality data, reliance on death certificate information or tumor registry data for job information, lack of information on confounding factors, and consideration of mixed histological types of brain and central nervous system cancers. These limitations may explain the inconsistency of some published observations.

## Conclusion

In conclusion, in this population-based case-control study we observed an increased risk of brain gliomas associated with employment in agriculture, rubber and plastic manufacturing, industries producing electrical and electronic equipment, and several industries or occupations that have a potential for exposure to gasoline or solvents. These observations are consistent with a majority of previous studies. In addition, we also observed an increased risk of brain glioma for employment in the apparel and other textile industries and in plumbing, heating, and air conditioning industries. Because chance cannot be ruled out as a possible explanation, these associations warrant further investigation.

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